A STUDY OF THE DEATHS ASSOCIATED WITH ANESTHESIA AND SURGERY*

BASED ON A STUDY OF 599,548 ANESTHESIAS IN TEN INSTITUTIONS 1948–1952, INCLUSIVE

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FOREWORD

ANESTHESIA IS AN adjunct to the care of the patient; hardly ever is it an end in itself, except where it is the principal physical tool used in the study and treatment of mental illness or where, for another example, nerve blocks are used in the treatment of paresthesias or circulatory disorders. In such limited cases, anesthesia is perhaps an end in itself. This study, however, is concerned with anesthesia as a part of the total surgical care of the patient. Anesthesia in this rôle is not of itself the therapeutic act which makes possible the correction of deformity, the restoration to health, or the staying of death. It merely makes possible the acts which can accomplish these things. We set down these truisms here, for it is our belief that one of the principal accomplishments of this survey is to show, within the precise framework to be described, the extent of the responsibility which must be borne by anesthesia for failure in the total care of the surgical patient.

The inseparability of anesthesia from the total care of the surgical patient is to us the compelling reason why surgeon and anesthetist, engaged as they are in a common task, cannot with profit pursue separate goals. The two great goals are facilitation of therapy (the surgical procedure in this case) and the patient's safety. Notwithstanding the frequent attempts to emphasize one of these aspects over the other, it is clear that in reality they merge into the single goal: a successful therapeutic procedure. Important, but far less so than facilitation and safety of the procedure is comfort of the patient. It is true that in certain abnormal patients, for example in extremely neurotic individuals or, for another example, in patients with severe mitral stenosis where mental agitation leads to pulmonary edema, that comfort is required to ensure safety; not often is this the case.

Inevitably and rightly the mounting data of this study have been widely discussed. Informed discussion has been encouraged during the accumulation of the data as a protection against oversight. From a methodological point of view it would, of course, have been better to have completed the study without any intermediate report to the participants. The data sample obtained each year was of such magnitude that it seemed desirable and necessary, from a humanitarian point of view, to pass along to the participants each year's findings, so they could act on the observations if it seemed desirable to them to do so. From a practical point of view it is not certain that all of the participating institutions would have continued with the study, which they did, without the annual report to maintain their interest. There is no evidence that such annual reporting influenced procedures in the local institutions, and there is evidence in the constancy of the anesthesia death rate over the course of the study that such annual reporting was without influence.

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TABLE I. *Anesthetists*

	Anesthesias Administered						
	1948	1949	1950	1951	1952	Total	% Total
Anesthesia Resident	39,800	47,800	48,500	49,600	55,900	241,600	40.3
Nurse	25,600	23,300	26,900	25,800	26,500	128,100	21.2
Surgeon	22,700	26,500	23,700	25,500	23,200	121,600	20.3
Anesthesia Specialist	11,000	10,400	13,300	12,800	14,700	62,200	10.4
Medical Student	3,700	5,500	5,900	5,200	3,700	24,000	4.0
Interne other than Anesthesia	5,100	4,200	5,300	3,400	4,200	22,200	3.6
Occasional Physician	400	400	40	90	30	960	0.2
	108,300	118,100	123,640	122,390	128,230	600,660*	100.0

*This is not in exact agreement with the 599,548 anesthesias referred to later. The discrepancy is apparently due to some hospitals attributing one anesthesia to more than one anesthetist. For instance, if the surgeon injects procaine for regional anesthesia and an anesthesia resident gives thiopental, then both surgeon and resident were counted in the one case. The error is less than 0.2 per cent.

We have no wish to exaggerate the accuracy of this study. It best fits into the category of a survey. No important conclusions in controversial areas have been arrived at where even a 100 per cent change in the data against the conclusion would alter the view. This is in recognition of the possibilities for error inherent in a study of this kind.

We hope that our conclusions give an accurate picture of the anesthesia situation within university hospitals of the United States at this period, where well-established departments of anesthesia exist. (Reasons for choosing a group of university hospitals for study will be presented below.) The fact that this carefully arrived at picture is, in several instances, not in accord with some current impressions has led, reasonably enough, to examination of the validity of the conclusions arrived at. We have welcomed such criticism.

A moment ago we spoke of the wide discussion evoked by this study. Possibly time will show that this interest and the self-examination stimulated by it will be the study's most valuable result. In any case, it may not be inappropriate to comment upon one or two directions such discussion has taken. Very often during such consideration, data at variance with those given here are presented. We make no claim to infallibility; but we have had an extraordinary opportunity to amass data within the limited framework of the university hospital. The data are as sound as we could make them. Whatever their shortcomings, we do not believe that casual clinical impression, unaided by painstakingly complete record keeping, can properly be used as an argument against these data. Nor do we believe that conflicting reports based upon the occasional voluntary and intermittent reporting of anesthesia deaths can be set against this study where *all* deaths from whatever cause were examined at the time they occurred and reported by those, both surgeons and anesthetists, who were on the spot when they occurred.

Again and again we have encountered confusion as to the fact that when we speak of a death associated with anesthesia and assigned to it, we mean just that, not a death attributed primarily to the patient's disease or to surgical error, or to other cause. One enthusiastic gentleman collected all deaths from all causes in a large area and tried to show that we had grossly understated the death rate owing to anesthesia. Such misunderstandings have driven us to what may seem to be a tiresome explicitness.

A recurrent misunderstanding has come out of the failure to realize that our objective here was to describe how things are, not how they could be or even how they should be, but *how they are*. Our hope was, that if we could establish how things

TABLE II. *All Technics.*

	All* Uses						
	1948	1949	1950	1951	1952	Totals‡	% Total
Inhalation†	57,500	62,200	65,100	59,900	64,700	309,400	44.4
Intravenous	21,600	27,000	31,300	33,900	40,100	153,900	22.1
Local	16,500	20,000	18,300	20,000	17,500	92,300	13.2
Spinal	12,300	12,400	12,700	10,300	11,000	58,700	8.4
Topical	7,900	10,700	8,900	9,400	9,300	46,200	6.6
Regional Block	3,800	2,500	3,900	4,000	3,000	17,200	2.5
Rectal	2,200	2,700	2,300	1,600	1,700	10,500	1.5
Caudal	1,900	1,900	1,800	1,700	2,100	9,400	1.3
	123,700	139,400	144,300	140,800	149,400	697,600	100.0

*Includes every technic used in a single anesthetic procedure.

†Count of the major inhalation technics used in a single anesthetic procedure.

‡Some small discrepancies between the totals in this Table and subsequent Tables (IV, VII, X) arise from rounding off the hundreds.

are, progress could then be made in the direction of how they should be. Participants have written in to say, "Most of our obvious anesthesia deaths resulted from mistakes of men in training; if our senior staff had administered all anesthesia, the data would be very different, etc., etc." Comments of this kind certainly miss the point of what we are trying to do.

Twenty-one physicians* and 11 secretaries worked on this report continuously for five years, thus there are involved 105 man-years of professional effort in which the material was painstakingly observed, recorded, gathered and checked. Each of the institutions invited to participate did so and remained with the study until the end of it. We accepted the conclusions arrived at in the given institution; certainly we had no right to change diagnoses or to alter conclusions arrived at by the participants.†

In preparing this material for publication we have distinguished plainly between observed fact and our opinions. The participants in the study have gathered the tabular material. We take the responsibility for the opinions expressed. The two of us who have prepared the text are solely responsible for any errors it may prove to contain.

The study was made possible by the Medical Research and Development Board of the Army, first under the Chairmanship of Colonel William S. Stone and then under Colonel John R. Wood. Their insight into the need for this work from a military as well as civilian point of view and their loyal furtherance of it has constituted a fine example of how military support can be, and is, of substantial aid to civil medicine.

BASIS FOR THE STUDY

PURPOSE

The purpose of this study was to determine as accurately as possible the death rate (and why deaths occurred) attributable to anesthesia, whether due to agent or technic, or to their misapplications, and thus to assess the responsibility of the anesthetist in the total care of the surgical patient when failure occurred. To accomplish this, *all deaths* from January 1, 1948, through December 31, 1952, occurring on the surgical services of ten participating university hospitals, were appraised. We have, therefore, of necessity, accumulated

* These numbers represent positions. While there was good constancy in the group, there was some shift of manpower, shown in the list of participants.

† The data of Table XXVII contained an error of cataloging by one or two of the participants. Even so, the data are shown both as sent in and as corrected.

TABLE III. *Inhalation Anesthesia*

Agents Primary* Uses	1948	1949	1950	1951	1952	Totals	% Total
Nitrous Oxide-Ether	13,300	14,600	14,600	14,600	13,000	70,100	25.4
Ether	10,600	12,800	14,000	14,900	15,400	67,700	24.6
Cyclopropane	5,800	6,400	8,600	7,200	6,100	34,100	12.5
Ethylene	5,400	5,500	5,700	5,600	7,000	29,200	10.5
Nitrous Oxide	5,400	6,300	6,300	4,300	3,900	26,200	9.5
Vinyl Ether-Ether	2,100	2,700	3,000	2,500	2,600	12,900	4.8
Ethylene-Ether	2,700	2,200	1,300	800	700	7,700	2.8
Vinyl Ether	2,200	1,400	1,200	1,900	900	7,600	2.7
Cyclopropane-Ether	1,400	1,700	1,800	1,200	1,200	7,300	2.6
Cyclopropane-Nitrous Oxide-Ether	700	1,000	1,300	1,400	1,200	5,600	2.0
Cyclopropane-Nitrous Oxide	400	500	200	200	400	1,700	0.6
Trichloroethylene-Nitrous Oxide	—	—	—	130	1,400	1,530	0.5
Ethylene-Cyclopropane	200	300	400	300	100	1,300	0.5
Trichloroethylene	—	—	—	110	600	710	0.3
Chloroform	—	—	—	220	300	520	0.2
Other	100	200	700	200	300	1,500	0.5
	50,300	55,600	59,100	55,560	55,100	275,660	100.0

*"Primary Agent"—Agent used for principal effect and for greater part of duration of anesthesia.

information concerning deaths associated with surgery, as well as anesthesia.

The desirability of this study is based upon (a) the belief that anesthesia has an unnecessarily high death rate; (b) our inadequate knowledge of where the dangers lie in making choices in the field of anesthesia, and (c) the belief that the study itself, by directing attention to these matters, would lead to sharper criticism of existing practices with improvement in them.* Moreover, we had hoped that the data obtained should make clear which agents and technics are desirable and which undesirable. At the conclusion of the study it is apparent, because of the very widespread practice of employing several to many agents in a single anesthesia performance, that comparative death rates for given agents become significant only when they are associated with rates very different from other agents. We must emphasize that the principal labor of this study was to find out how things are, what the situation is, not what it ought to be. But it is perhaps not necessary to leave the data in a condition as static as that statement suggests. Since this work has extended over a period of years, it would seem foolish not to examine the data for trends. This we have done, and have summarized this material at the end.

* Several of the participating institutions have stated that they have found the benefits of this work such that they plan to continue to examine their clinical performance in this way.

BACKGROUND

Previous information on background has been meager for several reasons: the difficulty of achieving accuracy in this field, and the fact that death rate could be many times as high as it needs to be, yet this fact not be evident in the experience of one or two individuals, and finally, because no such previous attempt, of this type or on this scale, has been made. Clearly, a mass attack was essential if the truth was to be discovered.

We are not aware of any other study of anesthesia death rate where all deaths on the surgical services have been examined. We believe it is only with such completeness that anything like accuracy can be approached. We are, of course, familiar with the other published estimations of anesthesia's death rate. And these are valuable in that they have served to direct attention to the problem. Several shortcomings are,

TABLE IV. *Inhalation Anesthesia*

	Technics Major* Uses						
	1948	1949	1950	1951	1952	Totals	% Total
Closed (Circle Filter)	28,700	32,000	37,700	32,900	30,000	161,300	52.2
Semi-open or Semi-closed	13,800	15,100	12,900	16,900	21,900	80,600	26.0
Open	11,400	8,100	8,700	3,400	6,300	37,900	12.3
Open with Insufflation	1,000	5,300	4,800	6,000	6,000	23,100	7.5
Closed (to-and-fro filter)	2,500	1,600	1,000	600	500	6,200	2.0
	57,400	62,100	65,100	59,800	64,700	309,100	100.0
Controlled Respiration	1,100	1,300	2,300	4,800	3,700	13,200	4.3
Assisted Respiration	—	100	100	200	200	600	0.2

*Count of the major inhalation technic used in a single anesthetic procedure.

however, often common to these studies: (a) No effort is made to assign cause to all deaths. (b) They deal only with deaths arising from flagrant error or accident (mix-up in gas tanks, aspiration of vomitus, and so on). (c) The reports are made by a surgeon *or* by an anesthetist, not by both working as a team. (d) The reports are voluntary and partial. (e) The data were not compiled at the time they arose, but from hospital records grown cold. (f) The samples are too small in number and too limited in scope (often one man's data) to have general applicability. (g) They have often been made to prove a point, that one agent is better than another. We hope we have avoided these obvious errors in this study.

University hospitals were chosen for several reasons. The places for study and the personnel were chosen because it was believed they represented typical university practice. Admittedly, "typicality" represents a judgment hard to verify. There are in the United States approximately 2700 non-profit "general and special short term" hospitals,* apart from governmental and proprietary hospitals. The university hospital is in this category. In all of these hospitals some 5,000,000 anesthesias are carried out per year, and in our sample we have gathered 120,000 per year, or about 2.5 per cent of the total, to give an idea of the relationship of our sample size to the whole body of voluntary, non-profit hospital material.

In choosing university hospitals we wanted to get as much uniformity in the material of the participating hospitals as possible, where high standards of medical care exist. Doubtless this could have been achieved by choosing private clinics; but among the difficulties with such a choice is the fact that there are not enough large private clinics scattered throughout the country, and representative national distribution was one of our goals. Veterans' hospitals or military hospitals would not have offered enough women and children. Comparable difficulties were present with other special groups of institutions. The university hospital seemed, therefore, to offer an opportunity to study the problem with large numbers under the best circumstances available and with a national spread. Various suggestions have been made from time to time that such and such a hospital should not have been included, or so and so should have been included. At the end of the study, we still do not believe we could have made a better choice of ten institutions with a national spread. The university hospital had the further advantage of permitting study of the performance of physicians in training, and of nurse anesthetists in comparison with physician specialists within the narrow limits possible in such a comparison.

* As recorded in *Hospitals*, **24**: 58, part II, June, 1950.

TABLE V. *Intravenous Thiopental Sodium (Pentothal) Anesthesia.*

	All Uses						
	1948	1949	1950	1951	1952	Totals	% Total
As Primary Agent							
Thiopental-Nitrous Oxide	9,500	10,500	12,100	14,200	16,700	63,000	43.6
Thiopental-Nitrous Oxide "Curare"	2,400	2,200	2,700	3,400	4,400	15,100	10.4
Thiopental	2,300	2,700	2,500	2,500	4,000	14,000	9.7
Thiopental-Ethylene	500	1,100	2,200	2,400	2,300	8,500	5.9
As Supplementary Agent							
Thiopental	4,600	7,300	7,000	7,800	7,600	34,300	23.7
Thiopental-combinations	1,000	900	1,900	2,600	3,300	9,700	6.7
	20,300	24,700	28,400	32,900	38,300	144,600*	100.0

*Total differs from total intravenous in Table II, since less used agents (e.g., thiamylal sodium, "Surital", pentobarbital sodium, "Nembutal") are here excluded.

At the end of each year we sent from the central office to those concerned, summaries of the year's chief findings. Twice in this time the participants have assembled for first-hand discussion. Two drafts of the final report have been sent to all participants.

THE PLAN

Six years ago it was therefore proposed that in ten of the major university hospitals in this country two physicians work with adequate secretarial assistance, one being a surgeon and the other the chief anesthetist of the institution, or his close associate. Over a full five-year period these individuals carefully examined *all* deaths of surgical patients and reported the data described below to the responsible investigators. In the five years of data collection, three reports per year, each covering the preceding four months, *i.e.*, a total of 15 reports from each participating institution, were sent in.

KINDS OF DATA COLLECTED

ANESTHETIC AGENTS AND TECHNICS

The number of agents, routes of administration, and technics were recorded according to the classifications shown in the tables. Where two (or more) *routes* of administration were used in a single anesthesia, the case was counted under the proper subheading of *each* route, and also under the proper sub-heading of "Combination of Routes."

An agent was counted as the *primary agent* if it was used for the chief effect and the greater part of the duration of the anesthesia. Any other is counted as a *secondary agent.*

Under the heading, "Combination of Routes," the matter of which was the primary or secondary agent was disregarded. If more than two routes were used, the combination was counted under the subheading of the two most important routes. Rectal anesthesia combined with another route was counted only under the heading "Rectal," where the combination was specified. Not enough information was gleaned from the "Combination of Routes" data to justify the use of space to present them.

Wherever "Other" appeared, only the number of cases was reported, unless one of the items lumped together under "Other" exceeded 10 per cent of the total group (*e.g.*, unless dibucaine hydrochloride [Nupercaine] was the agent for more than 10 per cent of the spinal anesthesias). If so, this agent was listed separately. Occasionally, in the case of agents having special interest, as tetracaine (Pontocaine) for local or regional anesthesia, detailed information has been given even though they made up less than 10 per cent of the uses.

See the collected tables for the details of listing and totalling.

TABLE VI. *Rectal Anesthesia*

	Principal Agents All Uses						
	1948	1949	1950	1951	1952	Totals	% Total
Tribromoethanol (Avertin)							
Alone	500	800	500	350	500	2,650	26.0
With various inhalation agents	700	1,300	1,000	400	150	3,550	35.0
With ether	200	100	120	500	800	1,720	17.0
With nitrous oxide	350	230	260	200	90	1,130	11.1
With procaine	100	130	150	50	1	431	4.2
With tetracaine (Pontocaine)	70	130	170	50	——	420	4.1
(Pentothal) Thiopental	60	20	40	70	80	270	2.6
	1,980	2,710	2,240	1,620	1,621	10,171*	100.0

*Differs from Table II since less used agents (e.g., pentobarbital sodium, ether) are here excluded.

In order to find out whether each of the participating hospitals treated about the same surgical problems, a sample of certain key operations was gathered and totalled over a two-week period three times a year for the five years. Thus it was assumed that if about the same percentage of gastric resections was carried out, that a comparable percentage of appendectomies would be involved in the institutions being compared, etc. These somewhat abbreviated samples of surgical practice gave the information sought as well as a complete itemization would have done.

The sampling of operations was done according to the following tally of operations: intracranial; intrathoracic (lobectomies, pneumonectomies, other); intra-abdominal (gastric resections, other—excepting inguinal hernias); genito-urinary major procedures (prostatic or renal surgery) and minor procedures (cystoscopies, circumcisions); on head, major and minor; on neck, major and minor; on chest wall, major and minor; on abdominal wall, major (including hernias) and minor; on extremities, major procedures (open reductions, bone grafts, joint surgery of long bones, etc.—including operations on the spine) and minor procedures (drainage of minor abscesses, operation on digits, etc.); obstetric procedures (vaginal delivery, cesarian sections).

The totals of these operations for each two-week period were compared for each institution. It was evident on inspection that the material involved in each of the participating hospitals was reasonably comparable and reasonably homogeneous, though by no means identical. This approximate homogeneity gives us more confidence that our data do represent university hospitals more generally than would have been the case if each hospital had had an extremely specialized program of surgery.

As a further device for ready checking of the comparability of the participating hospitals, and as some indication of comparable standards (also made evident in the similarity of the percentages of deaths assigned to the several death categories, referred to earlier), the number of admissions, operations, and deaths on each of the various surgical services, as, for example, general surgery, neurosurgery, orthopedics, urology, obstetrics, etc., were tallied for each four-month report.

In the beginning, we had expected that it would be of interest to compare institutions. In the end we found that there was not enough of interest in these data to justify the space required to present them in detail. The data were useful in indicating reasonable homogeneity of the material (Table XIV B).

CAUSES AND CLASSIFICATIONS OF THE DEATHS

The deaths of all surgical patients, including the surgical specialties (orthope-

TABLE VII. *Spinal Anesthesia*

	Agents All Uses						
	1948	1949	1950	1951	1952	Totals	% Total
Tetracaine (Pontocaine)	6,500	6,900	8,400	6,700	7,800	36,300	61.7
Procaine	2,500	2,400	2,300	2,300	1,600	11,100	18.9
Dibucaine (Nupercaine)	2,400	2,100	1,300	850	600	7,250	12.3
Procaine-tetracaine	700	1,000	600	450	400	3,150	5.3
Piperocaine (Metycaine)	30	130	100	100	30	390	0.7
Other	100	100	100	50	300	650	1.1
	12,230	12,630	12,800	10,450	10,730	58,840	10.00

dics, urology, neurosurgery, gynecology, obstetrics, pediatrics, etc., and accident ward surgical admissions) and the newborn (whether the patient had been anesthetized or not) were classified according to categories. (A representative, but not complete, list of typical examples will be given.) It must be made clear at once that decision as to the cause of the death in question was made in the institution where it occurred and when it occurred as soon as the relevant data were assembled. Unfortunately, it is not always possible to be exact as to the cause of death. The decisions are as accurate as careful study and thought could make them. Designations were not changed in the central office.

A single *primary* cause for each death was decided upon and entered in the appropriate column of the tables. The totals of the "primary" causes thus equalled the total number of deaths. In addition, certain deaths had more than one cause, *i.e.*, one "primary," plus one or more "contributing" causes. These were entered in the appropriate place. The totals of the "contributing" causes vary, depending upon how many deaths involve more than one cause. The classifications of cause of death follow:

Patient's disease. Patients were placed in this category when death was thought to be due to unavoidable progression of the patient's disease, whether surgery was justifiably avoided or if adequate uncomplicated surgery occurred. A patient's death was not attributed primarily to "patient's disease" unless none of the other causes listed below was present.

Error in diagnosis. (a) No operation done. This classification applied when an error in diagnosis contributed directly to the death of patients not operated on. For example, a patient died of generalized peritonitis from a ruptured appendix while being treated conservatively under an erroneous diagnosis of acute hemorrhagic pancreatitis, or a patient died of retroperitoneal infection from traumatic retroperitoneal rupture of the duodenum undiagnosed and treated conservatively.

(b) Operation done. This classification applied when an incorrect operation was done, based upon an incorrect diagnosis, and death ensued from this. For example, a diagnosis of acute appendicitis was made and simple appendectomy carried out, while the patient's illness and death were due to perforated peptic ulcer undiagnosed and not discovered at operation.

Error in surgical judgment. This category included mismanagement of the patient. For example, (1) failure to digitalize when clearly indicated; failure to administer adequate blood in shock (although blood was available); premature discharge of patient, leading to death from poor care; (2) if the patient died as a result of error in judgment of the type of operation that should have been performed.

Error in surgical technic. This classification applied when the patient died from complications attributable to errors in tech-

TABLE VIII. *Spinal Anesthesia*

	Technics All Uses						
	1948	1949	1950	1951	1952	Totals	% Total
Single Dose							
Heavy Solution	11,400	11,400	11,500	9,000	9,700	53,000	90.3
Light Solution	200	300	300	500	400	1,700	2.9
Unspecified (Hosp. D.)	—	200	500	500	600	1,800	3.1
Continuous or Multiple Dose	700	500	400	300	300	2,200	3.7
	12,300	12,400	12,700	10,300	11,000	58,700	100.0

nic. Examples: (1) Death attributable to postoperative hemorrhage caused by the slipping of a tie or failure to ligate a vessel, (2) death attributable to infection, whatever the cause, if it was not present at the time of operation and could have been related to the operation, and (3) death attributable to hemorrhage at a suture line or leakage of the contents of a hollow viscus.

Anesthesia death. This classification applied both when anesthesia was directly responsible for a death and also when anesthesia was considered to have been a very important contributing factor. This distinction was a matter for informed judgment to settle. In order that the data not be shaded in either direction and since this study was primarily directed at anesthesia as a cause of death, we have in this category carefully distinguished in the over-all data between deaths due primarily to anesthesia and to anesthesia as an important contributing cause of death, and have recorded the numbers involved in each group (Table XXVI, and discussion on page 23). We are chiefly interested in the cases where anesthesia is an important factor in the death. This includes both the primary and the contributory groups.

The following examples were given to the participants, but were not intended to cover all possibilities, nor were they to serve as any sort of subclassification of anesthesia deaths. They illustrate, as a guide to judgment, some of the kinds of situations that lead to placing a death in this classification. Examples: (1) Error in the choice of anesthetic agent or technic (examples: cyclopropane in hyperthyroidism with cardiac arrest; high spinal in a seriously hypertensive patient). (2) Inherent toxicity of agent; examples: ventricular fibrillation or acute yellow atrophy of the liver from chloroform. (3) Abnormal sensitivity; example: fatal depression from a small dose of a barbiturate. (4) Error in administration of agent or technic; examples: overdosage of ether; inadequate ventilation of the lungs in open thoracic surgery due to obstruction of the airway by pus, or to inadequate ventilation as a result of mismanaged positive pressure in the airway; inadequate oxygen; injection of epinephrine in a patient under cyclopropane; mistaken identity as, mix-up in gas tanks; perforation of trachea by endotracheal tube. (5) Inadequate supervision; example: as in teaching cases. Here, of course, the fatal error might be one of those listed above or below. (6) Error in preoperative, operative, or postoperative care of patient while under the anesthetist's care; example: vomiting with suffocation from aspiration, or delayed death from pneumonia or lung abscess as a consequence of aspiration. (7) Explosion (electrostatic, cautery, diathermy, flame, etc.). (8) Miscellaneous situations; example: (a) death during induction, before surgery had been started, (b) during surgery or before recovery from anesthesia if no other cause was present (this constituted a presumptive anesthesia death), (c) where noxious

TABLE IX. *Local or Regional Anesthesia.*

	1948	1949	1950	1951	1952	Totals	% Total
Agents All Uses							
Procaine	19,600	20,400	20,900	23,100	20,300	104,300	85.9
Piperocaine (Metycaine)	2,000	2,200	1,800	1,600	1,300	8,900	7.3
Procaine Supplement	800	400	400	500	1,200	3,300	2.7
Lidocaine (Xylocaine)	———	———	———	600	1,800	2,400	2.0
Tetracaine (Pontocaine)	150	200	200	700	300	1,550	1.3
Dibucaine (Nupercaine)	———	———	———	140	50	190	0.2
Other	130	90	90	150	300	760	0.6
	22,680	23,290	23,390	26,790	25,250	121,400*	100.0
Technics							
Local Injection	16,500	20,000	18,300	20,000	17,500	92,300	77.7
Regional Block	3,800	2,500	3,900	4,000	3,000	17,200	14.4
Caudal	1,900	1,900	1,800	1,700	2,100	9,400	7.9
	22,200	24,400	24,000	25,700	22,600	118,900*	100.0

*Totals differ since: (a) more than one agent was given by a single technic in one patient, or (b) all agents used were listed whereas only the major regional technic was listed.

reflexes were a cause of death under anesthesia (endotracheal intubation with sudden cardiac failure), (d) vascular accident during induction in a hypertensive* patient or vascular thrombosis following hypotension related to anesthesia, (e) change of position under anesthesia, with sudden circulatory collapse and death, and (f) suffocation from foreign bodies, packs left in the airway.

THE DATA

The data are presented in the accompanying tables.

ANESTHETISTS

DISCUSSION OF DATA ON AGENTS AND TECHNICS

Table I, Anesthetists. It may come as a considerable surprise to some that in these ten university hospitals with well-established departments of anesthesia, a fifth of all anesthesia is administered by nurses, and nurses account for twice as many anesthesias as physician specialists in anesthesia. It is true that the physician certainly carries, case for case, a greater load of difficult cases than does the nurse in several of the participating hospitals. However, in some of the hospitals there is no difference in the type of cases anesthetized by nurses and physicians. There are not enough physicians to provide anesthesia in this country; whether there ever will be can only be a matter of opinion at this time. Current trends are probably indicated by the fact that while the total number of anesthesias administered in this collection of hospitals increased 18 per cent (108,000 to 128,000 per year) over the five-year period of study, the cases administered by nurses increased only 3.5 per cent, whereas, those given by physician specialists increased 34 per cent and those by anesthesia residents increased 40 per cent. Another way of looking at these data as well as many of those to follow, is to consider, not as above, the change in percentage over the five years of the study, but in terms of rates per year. These can then be compared. Thus, in 1948 the nurse anesthetist administered 25,600 out of a total of 108,300 anesthesias, or 24 per cent of the total. In 1952, she administered 26,500 out of 128,230, or 21 per cent, a decrease of 3 per cent. Each

* Many patients weakened by heart disease, say, or other serious disability, die when some epidemic comes along. Their deaths are attributed to the epidemic disease, yet healthier people survived the epidemic. The epidemic was the death-precipitating factor, just as in our case, anesthesia was. We have followed common practice.

TABLE X. *Topical Anesthesia.*

	Agents All Uses						
	1948	1949	1950	1951	1952	Totals	% Total
Cocaine	2,600	4,600	4,500	4,500	4,100	20,300	43.7
Cocaine Supplement	600	1,100	1,400	2,100	2,500	7,700	16.6
Tetracaine (Pontocaine)	2,700	2,100	1,300	1,100	1,000	8,200	17.7
Tetracaine Supplement	400	1,800	1,000	800	500	4,500	9.6
Dibucaine (Nupercaine)	1,400	600	———	150	850	3,000	6.5
Piperocaine (Metycaine)	———	200	100	———	40	340	0.7
Ethyl Chloride	50	10	25	520	25	630	1.4
Other	100	350	600	400	300	1,750	3.8
	7,850	10,760	8,925	9,570	9,315	46,420	100.0

approach gives interesting and special information. For brevity, only the former will be used in the data to follow. The basic data are all provided so that the second type of information can easily be obtained.

It is reassuring to find the occasional physician administering so few anesthesias. The 20 per cent carried out by the surgeons is to be accounted for largely by topical and local infiltration anesthesia.

Table II, All Technics. It is evident that inhalation anesthesia remains of principal importance, accounting, as it does, for nearly half of the uses. It is interesting to observe that the use of intravenous anesthesia has nearly doubled in the five-year period of study, while the spinal technic appears to have lost some ground. It was a considerable surprise to us, and may be to others, to find spinal anesthesia accounting for less than 9 per cent of the uses.

It perhaps should be explained that the total of 697,600 exceeds the number of anesthesias, since more than one technic is often used in a given case; that is, the same patient can receive both inhalation and intravenous anesthesia, etc.

Table III, Inhalation Anesthesia, Agents. There are a number of interesting observations to be made from this table: The use of ether as a primary agent has increased 45 per cent in the five years (and the increase has been steady) as compared with a decrease for cyclopropane in the last two years, or essentially no change in the use of cyclopropane if the first and last years are compared. (A preservation of the same numerical status represents in fact a decrease, since the number of anesthesias increased 18 per cent during the five years of this study.)

If all uses of ether, alone as well as in combination, are added together, it can be seen that this agent was used in 62 per cent of the inhalation anesthesias, whereas cyclopropane was used in 18 per cent.

Table IV, Inhalation Anesthesia, Major Technics. The long-tested and soundly established, closed, circle filter arrangement for administering inhalation anesthesia has justly acquired and held an important place. It is not so evident why the semi-open technic, which is so wasteful of gases, should have increased nearly 60 per cent in the five-year period. This may be related to the current practice of using nitrous oxide in conjunction with muscle relaxants or intravenous anesthesia, as indicated in Table V. The increased use of intravenous anesthesia shown in Table V was also shown in Table II. Probably the three-fold increase in "controlled respiration" shown in Table IV is necessitated by the wide use of the muscle relaxants.

The sharp downward trend in use of the to-and-fro filter (2500 to 500 cases) in the five-year period reflects a general dissatisfaction with this technic, probably owing, in large part, to the tendency of this filter

TABLE XI. *Endotracheal Intubation.*

Under	All Uses 1948	1949	1950	1951	1952	Totals	%* Tota
Inhalation Anesthesia	9,400	12,400	12,800	11,500	11,600	57,700	71.8
Intravenous Anesthesia	2,800	2,400	3,300	6,000	7,200	21,700	27.0
Regional or Tropical Anesthesia	200	300	300	100	100	1,000	1.2
	12,400	15,100	16,400	17,600	18,900	80,400	100.0
Per cent of Primary Inhalation (Table III) Plus Primary Intravenous (Table V) Anesthesias Intubated	18%	20.5%	20.5%	22.4%	22.9%		

*% Total: % of total number intubations done.

to heat up to a troublesome degree, as well as to inconvenience of the apparatus.

Table VI, Rectal Anesthesia. The use of rectal anesthesia appears to be nearly stationary. If there is a change it is in the direction of a decline in use. See also Table II in this connection.

Table VII, Spinal Anesthesia, Agents. Over 85 per cent of all spinal anesthesia is accomplished with tetracaine (Pontocaine) or procaine or their combination. A sharp fall in the use of dibucaine (Nupercaine) is evident over the course of this study; at the end it is down to one-quarter what it was at the beginning of the study.

Table VIII, Spinal Anesthesia, Technics. While the continuous or multiple dose technic never carried more than a small percentage of spinal anesthetics, there appears to have been a decline in its employment over the five-year period of the study. The extensive use (90 per cent) of heavy solutions in spinal anesthesia is doubtless a reflection of the common experience that these are more controllable than light solutions.

Table IX, Local or Regional Anesthesia. It is reassuring, because of its established low toxicity, to find that procaine continues to provide for more than 85 per cent of local or regional anesthesia.

Table X, Topical Anesthesia, Agents. Cocaine used for primary topical anesthesia or as a supplement has had a wide use, steady over the last four years, whereas the topical use of tetracaine (Pontocaine) primarily has been halved in the five-year period of this study. It can be seen in Table X that the number of uses of cocaine for topical anesthesia was for 1948 out of line with the subsequent four years. We believe the number for that year to be incorrect, but have recorded it as sent in. Efforts to resolve the matter have not been entirely satisfactory, but it appears that the explanation is in large part to be attributed to misunderstanding during the first year of the study that patients cocainized by endoscopists (for which no anesthesia records were kept) were to be counted.

Table XI, Endotracheal Intubation. This technic is used principally with inhalation anesthesia. It is interesting to observe a rapid increase (more than double) in its use as an adjunct of intravenous anesthesia, probably a reflection of the employment of this combination with muscle relaxants.

In conjunction with endotracheal intubation there is an increasingly great tendency to use inflatable cuffs on the tube. We have long believed[1, 2] that while these are valuable in certain special circumstances (notably transthoracic esophageal resection, or where vomiting or regurgitation of gastric or bowel contents may be a problem, and where abscesses in the upper airway must be drained under general anesthesia), they carry a hazard, morbidity and mortality of their own. Accordingly, we were interested to observe that two of the 384 anesthesia deaths were due to cuffs. (This is not the first report of death due to this device.)

TABLE XII. *Incidence of Use and of Death Associated With "Curare"* by Year.*

	1948	1949	1950	1951	1952	Total or Average
Anesthesia which Included "Curare".	6,000	6,800	9,100	10,900	11,300	44,100
Incidence of Use of "Curare".....	1 : 18	1 : 17	1 : 14	1 : 11	1 : 11	1 : 14
Incidence of "Curare Death".....	1 : 380	1 : 360	1 : 320	1 : 390	1 : 420	1 : 370
Incidence of Use of "Curare" in All "Anesthesia Deaths".....	1 : 5	1 : 4	1 : 3	1 : 2.5	1 : 2.5	1 : 3

*"Curare" in this and other Tables refers to all muscle relaxants. Data on specific muscle relaxants are presented in Table XXII.

Of these two cases, one cuff got inflated with nasal oxygen, with fatal rupture, and the other broke during lobectomy for abscess and allowed the dependent lung to be suddenly flooded with detritus. These deaths are not an adequate argument for abandonment of this useful tool; but they are an indication for having a well-thought-through reason for using cuffs.

SPECIAL DISCUSSION OF MUSCLE RELAXANTS ("CURARE")

The muscle relaxants have been singled out from the other agents and technics for particular discussion because of their newness, because of their greatly increasing use, and because their employment appears to be associated with certain anesthetic hazards not yet entirely clear, nor completely appreciated. And finally, evidence will be given that where the muscle relaxants are involved, an appreciable increase in the anesthesia death rate is presented. On the other hand, we do not have evidence that the muscle relaxants affect the over-all death rate in surgical patients, for to get this kind of evidence we would have needed more extensive (and expensive) data than were gathered.

The word, "curare," as used below, refers to all of the muscle relaxants included in this study. Data on "curare" agents are given in Tables V, XII to XXV, inclusive, and XXX to XXXIII, inclusive.

It must be stated at once, and as plainly as possible, that we refer to "curare deaths," meaning deaths associated with "curare," *i.e.*, with the use of muscle relaxants. We have not made, nor do we make, any claim that any specific patient has been killed by the use of a muscle relaxant. Unfortunately, the times are relatively few when one can obtain *proof* that any drug has killed a given patient. We do not *know* that "curare" has killed a single patient. In this as in other fields in medicine one is obliged to draw inferences as sound as he can from the available data. Many, one could say most, of the advances in medicine have been based upon exactly that procedure.

This section seems to us to offer a good occasion to reverse in part the usual procedure for presenting data; that is, we shall say straight out which data seem to us to have importance and which do not, so the reader can bear this in mind on his first examination of the material. (1) The simple division of the data into anesthesia with and without "curare" (Table XIII) makes the muscle relaxants appear very bad, unreasonably so, we think, for many trivial procedures (as under local anesthesia) dilute the "non-curare" data. Since the difference, however, is six-fold, it is a plain stop-look sign. (2) Table XXXII supports the admonition just given, for in no other instance where similar "with" and "without" data are compared, is the difference so striking as with "curare." The nearest is

TABLE XIII. *Total Incidence of "Curare" Use and Associated Death.*

Total Number Anesthesias	599,500
Number Anesthesias in which "Curare" Used (1 : 14)	44,100
Frequency of Death Related to Anesthesia	
Anesthesias Which Did Not Include "Curare" (266)	1 : 2100
Anesthesias Which Included "Curare" (118)	1 : 370

TABLE XIV. *A. Surgery and Associated Anesthesia Deaths With and Without "Curare."*

Presence or Absence of Muscle Relaxant	Status of Surgery	Total Number of Patients* (Living and Dead)	Number of Anesthesia Deaths	Per Cent of Anesthesia Deaths	Anesthesia Death Rate
No "Curare"	None		35	13	
	Minor	349,939	69	26	1 : 5071
	Major	205,519	162	61	1 : 1270
"Curare"	None		21	18	
	Minor	27,777	12	10	1 : 2314
	Major	16,313	85	72	1 : 192
Totals		599,548	384		

*Based upon the assumption that the same percentages of major (37) and minor (63) surgery existed in the "curare" and no-"curare" group as was true for the over-all data (see Table XIV B).

ether, where the difference is three-fold as opposed to six-fold with "curare." We do not wish to dwell on this unreasonably. (3) Take the situation (Table XVI) where the combination of thiopental and "curare" is considered. There was a great and steady improvement throughout the study in the incidence of death associated with thiopental, but the rate for "curare" remained constant. We believe these to be important supporting data. (4) Take the somewhat simplified situation where the patients died during *induction* of anesthesia (Table XIV): when "curare" was used the rate is 1:2000, when not used, the rate is 1:15,500. (It is 1:10,800 when only general anesthesias are considered.) None of these four items adds up to proof; they are all in the same direction and they all suggest that "curare" may be causing trouble. (5) The foregoing is supported by the failure of experience of the individual to protect (Table XIX), and by the failure of experience of the clinic to protect (Table XXIII). This is in line with what one would expect if the basic problem were one of inherent toxicity. Also in line with this is: (6) The ratio of the death rate of patients in good physical status (good risk) to the death rate in poor status is the same in the no-"curare" and the "curare" groups (Table XVII). (7) Examination of death rate associated with major operations (Table XIV, A) with and without "curare" compare as 1:192 to 1:1270, again a six-fold difference, unfavorable to "curare." (8) The combination of ether and "curare" (Table XXXIII) appears to be the worst of any studied, cyclopropane and "curare" less bad, and the combination of "curare" and thiopental least bad of the three. (9) It has not heretofore been recognized that death from "curare" can be other than respiratory. In Table XXV, cardiovascular failure, despite artificial respiration of a generally effective type, appears to be the cause of death. This is in agreement with experimental work in our laboratory (Normann and Löfström) on the ganglionic blocking effects of the three combinations. (10) Finally, we should like to say as plainly as we can that we do not believe Tables XXX, XXXI and XXXIII are of much help. They can easily be misleading.

B. Magnitude of Operations in the Ten Participating Hospitals.

Per Cent Major	Per Cent Minor	Total Number Anesthesias	Non-"Curare" Death Rate
28	72	75,400	1 : 2180
33	67	105,600	1 : 4000
35	65	69,000	1 : 2050
37	63	93,400	1 : 1540
37	63	88,300	1 : 1600
42	58	9,400	1 : 1180
43	57	38,800	1 : 1780
44	56	29,500	1 : 2090
46	54	59,300	1 : 3620
53	47	30,900	1 : 1810
Totals...37.2	62.8	599,500	1 : 2100

TABLE XV. *"Curare."*

	All Uses						
	1948	1949	1950	1951	1952	Totals	% Total
"Curare" with Various Agents							
Chiefly Thiopental (Pentothal)-Nitrous Oxide...	5,300	5,600	8,200	9,900	9,100	38,100	86.5
Chiefly Cyclopropane.....	500	500	220	500	700	2,420	5.5
Chiefly Ether.....	140	300	230	300	1,000	1,970	4.4
Chiefly Cyclopropane-Ether.....	100	400	400	200	500	1,600	3.6
	6,040	6,800	9,050	10,900	11,300	44,090	100.0

We present them because many want to see this material and because, in a negative way, they do illustrate an important point: That as long as many agents are used simultaneously in a single patient, it is not possible to get at a helpful estimation of death rate, and thus progress of this kind is blocked, unless one agent in the mixture has a death rate far greater than the others. "Curare" may be such an example.

"Curare" agents and associated deaths. There are no impressive differences between the rates in Table XXII. Not enough material is available to cast up any meaningful rates for the last three agents in the Table. It is interesting to observe, however, that deaths have occurred in association with all three of these agents. This is especially interesting for succinylcholine, the newest and at the moment most enthusiastically advocated agent. Quite possibly, as a consequence of its fleeting action, if for no other reason, it will prove to represent a major advance toward safety in the use of these compounds. We hope so. But until more nearly adequate data are in hand the drum beating could be muffled a little to advantage. The agent certainly merits careful trial.

The average "curare" doses used in the anesthesia death cases are (where the dose was stated) as follows: Tubocurarine chloride and "Intocostrin," 89 uses, average dose 15.2 mg.; "Syncurine," 24 uses, average dose 2.9 mg.; "Flaxedil," 2 uses, average dose 45 mg.; succinylcholine, 3 uses, average dose 197 mg.

We are well aware of the fact that most of the data of the kinds we are working with here can be dealt with only in a fairly broad way. Now if we stick to the practice of looking for broad relationship we can break down the 384 deaths (where it is agreed that anesthesia was of very great importance in the patient's death) as follows: In 266 of these no muscle relaxants were employed, with a death rate of 1:2100. In 118 deaths "curare" was used, with a death rate of 1:370 (Tables XII and XIII). Here, then, in the simplest terms, we have a situation where so far as we have been able to see, one factor has been changed and the death rate has increased nearly six-fold. There is no reason to give undue mathematical emphasis to whether the true ratio is three-fold or ten-fold. The important point is that in these data obtained throughout the United States and described in each of the ten institutions, something serious appears to happen when a muscle relaxant is added to the situation. (The absolute number of uses of "curare," as well as the incidence of use in "all anesthesia deaths" have doubled in the five years of this study [Table XII].)

A number of reasonable questions grow out of this: First, is this increase in death rate reported here common experience? The answer of many competent observers is: It is. One's ear need not be very close to the ground to hear of many examples of disaster associated with the use of muscle relaxants. One can no more demonstrate safety than he can the lack of it by casual

TABLE XVI. *"Anesthesia Deaths" Associated with Thiopental Sodium (Pentothal) and "Curare."*

	All Uses of Thiopental Without "Curare"			"Curare", All Uses		
Year	Uses	Deaths	Rate	Uses	Deaths	Rate
1948	15,200	21	1 : 720	6,000	16	1 : 380
1949	19,200	17	1 : 1100	6,800	19	1 : 360
1950	21,800	17	1 : 1300	9,100	28	1 : 320
1951	23,200	8	1 : 2900	10,900	28	1 : 390
1952	30,200	9	1 : 3400	11,300	27	1 : 420

clinical impression. The truth can be sought only in large masses of data carefully collected *at the time accidents occur.* The question* here is how many cases are needed to establish a difference between 1:370 and 1:2100? Though the problem is a complicated statistical one, it would be fair to say that even to have a 50:50 chance of detecting this difference, more than 2500 cases under each condition would have to be gathered. Thus the experience of a single individual is not likely to reveal the whole situation.

A second pertinent question is, are the two groups, *i.e.,* anesthesia with and without muscle relaxants, comparable? We have evidence to present which seems to indicate that they are, in certain respects. The time has long passed when most reasonable people would claim that the muscle relaxants are reserved for difficult or bad risk patients or patients in poor physical status. In any case, the data of Table XVII are positive evidence against any such conclusion. There it can be seen that 87 per cent who received "curare" were labeled *before anesthesia* as good risk (*i.e.,* good physical status) and 13 per cent as bad risk (poor physical status). These figures compare well with 89 per cent and 11 per cent, respectively, in patients who received no "curare." Certainly "curare" is not reserved for bad risk patients, *i.e.,* patients in poor physical status. The widespread custom of using the muscle relaxants for many trivial purposes is well known; *i.e.,* with plastic surgery on the skin, with operations on the fingers, on the toes, on the anus, and simply to facilitate endotracheal intubation as a routine.

We can ask the specific question: Can the anesthesia deaths be correlated with the risk of the patient, with his physical condition? It is possible to find a pertinent answer to this in Table XVII. Good risk patients die 4.7 times more often when "curare" is used than when it is not, and poor risk patients die 5.8 times more often when "curare" is used than when it is not. In this consideration it must be observed

TABLE XVII. *Physical Status.*

	Good (1, 2, 5)	Poor (3, 4, 6, 7)
"Curare" Deaths	49% 58 Cases	51% 60 Cases
All Patients* Who Received "Curare"	87%	13%
"Non-Curare" Deaths	59% 157 Cases	41% 109 Cases
All Patients* Who Received No "Curare"	89%	11%
Death Rate† of Patients Who Received "Curare"	1 : 660	1 : 96
Death Rate† of Patients Who Received No "Curare"	1 : 3100	1 : 560

*Based upon a 13,204 patient sampling made in 1952, from a two-week interval in each four-month period in all ten hospitals.

†Based upon the premise that the above sample of physical status distribution holds for the entire five years.

*We are indebted to Professor Frederick Mosteller for guidance here. Calculation for 50 per cent chance: To detect a difference between death rates $\frac{1}{370}$ and $\frac{1}{2100}$, suppose that the same size samples were used under both conditions. Using a 5 per cent level, then the "t" is

$$\frac{p_1 - p_2}{\sqrt{\bar{p}\,\bar{q}\left(\frac{1}{n} + \frac{1}{n}\right)}} = 2.$$

Then $p_1 = \frac{1}{370} = .0027$,

$p_2 = \frac{1}{2100} = .0005$, and

$\bar{p} = \frac{p_1 + p_2}{2} = .0016$.

$\bar{q}$ = approximately 1

Substituting these values, one gets:

$$\frac{.0022}{\sqrt{.0016\left(\frac{2}{n}\right)}} = 2 \quad \text{Solving, } n = 2600$$

TABLE XVIII. *Physical Status of 13,204 Patients (Two-Week Samples from Each of 3 Periods in 1952).*

Agent (Total Uses)	Good (1, 2, 5) Number	Good (1, 2, 5) Per Cent	Poor (3, 4, 6, 7) Number	Poor (3, 4, 6, 7) Per Cent
Ether (4276)	3,589	84	687	16
Nitrous Oxide (5646)	5,219	92	427	8
Cyclopropane (1920)	1,660	86	260	14
Ethylene (1504)	1,312	87	192	13
Vinyl Ether (770)	727	94	43	6
Thiopental (4269)	3,893	91	376	9
Spinal Technics (1348)	1,124	83	224	17
Regional & Topical Agents (1953)	1,647	84	306	16
All "Curare" (1402)	1,226	87	176	13
"Curare"-Pentothal (1094)	990	90	104	10
"Curare"-Nitrous Oxide (919)	818	89	101	11
"Curare"-Cyclopropane (228)	170	75	58	25
"Curare"-Ether (270)	232	86	38	14
Comparison of Anesthetists				
Physician-Specialist (1765)	1,550	88	215	12
Resident (6948)	6,025	87	923	13
Nurse (3188)	2,732	86	456	14
All Patients (13,204)	11,446	87	1,758	13

TABLE XIX. *Anesthesias, "Anesthesia Deaths" and Associated Anesthetists.*

A.

Anesthetist	All Anesthesias	"Non-Curare" Deaths	"Curare" Deaths
Anesthesia Specialist	11%	19%	18%
Anesthesia Resident*	48%	59%	63%
Nurse	21%	18%	19%
Surgeon	20%	4%	0
	100%	100%	100%

*Includes surgical residents on anesthesia and medical students.

B.

Anesthetist	Cases	Deaths	Ratio
Anesthesia Specialist	62,200	70	1 : 890
Anesthesia Resident*	287,800	233	1 : 1200
Nurse	128,100	70	1 : 1800
Total	478,100†	373	1 : 1300

*Includes surgical residents on the anesthesia service and medical students.

†Remainder of 599,500 anesthesias done by surgeon and occasional physician.

that patients in poor physical status die when no "curare" is used 5.5 times more often than good risk patients when no "curare" is used, and this is to be compared with the fact that when "curare" is used, poor risk patients die 6.9 times more often than good risk patients. Statistical testing shows that there is no significant difference between 5.5 and 6.9 here; therefore, we can say that poor risk patients are *not* selectively acted on by "curare." In this study all patients were separated and labeled as to "risk"; *i.e.*, as to their physical condition *before* anesthesia was undertaken. The patients were divided by all participants (except one who had a comparable system) into seven groups, of which the first four denote elective surgery (number one is a good risk, number two is a fair risk—not quite normal—as, for example, with a moderate hypertension; number three is a poor risk, with some serious lesion as, for example, a coronary thrombosis six months earlier, and number four is a desperately poor risk); numbers five, six and seven denote emergency surgery (number five is a good risk; *e.g.*, acute appendicitis in a previously healthy young man; number six is a poor risk, a severe hemorrhage without wound shock after an accident; number seven is a desperate risk, *e.g.*, multiple serious injuries with severe wound shock, following an accident). Risk numbers one, two and five were put together and called patients with a good physical status; risk numbers three, four, six and seven were put together and indicate a poor status. The above data offer strong evidence that "curare" is not simply causing trouble in patients with poor physical status. It is, of course, obvious that physical status alone is not the whole story, for severity of operation also becomes a factor in this situation. The ratio of death of good risk patients to bad risk is the same whether "curare" is used or not. It is possible that certain specific diseases might predispose to death from "curare." See the discussion below on sex relationships. These data, with others to follow, based upon large numbers, are a sharp

TABLE XX. *Time Relationships of "Anesthesia Deaths."*

	Time From Last Dose "Curare" to Fatal Episode or Death (118 Cases)		Time From Start of Anesthesia to Fatal Episode or Death "Curare" Cases (118 Cases)	Time From Start of Anesthesia to Fatal Episode or Death "Non-Curare" Cases (266 Cases)	
	Number Cases	Per Cent	Per Cent	Number Cases	Per Cent
Less Than 10 Minutes	27	23	11	28	10
10 Minutes to One Hour	31	26	24	95	36
More Than One Hour	39	33	65	143	54
Inadequate Records	21	18			
		100%	100%		100%

TABLE XXI. *"Curare" Deaths Associated With Sex, Race and Age.*

	Sample* Surgical Population	"Non-Curare" Deaths	"Curare" Deaths
Male	43%	52%	68%
Female	57%	48%	32%
White	70%	73%	68%
Colored	30%	27%	32%
Average Age	41 yrs.	40 yrs.	50 yrs.

*9300 patients in hospitals on April 1, 1950, and February 1, 1952.

warning of a possible specific inherent toxicity in the "curare" agents studied, not primarily related to the condition of the patient.

The next question to be asked is, what is the time relationship of use of "curare" to death? Bearing in mind the well-known hazards in the area of cause and effect relationships, it is interesting, but not more, to learn as we can from Table XX that among deaths, 23 per cent died within ten minutes of the last injection of "curare." The data are not really very comparable, for "curare" was not used in many cases at the beginning of anesthesia. In so far as they are comparable, the percentages look quite similar and cloud the time relationship issue.

Another pertinent question is whether the deaths associated with the use of "curare" occur primarily with major surgery. Table XIV A, comparing anesthesia death rate for major operations with and without "curare," shows a statistically significant difference if the assumption made (see footnote to Table XIV A) is correct. For this assumption to be incorrect there would have to be nearly a seven-fold difference in the division into major and minor groups. There were 21 anesthesia deaths during induction of anesthesia, before surgery, in the 44,090 "curare" cases, 1:2000; and only 35 anesthesia deaths, before surgery, in the 555,458 "non-curare" cases, 1:15,500. It is more informative if, in this large group, only the patients receiving general anesthesia are included; that is, 68 per cent (Table II) of the total, or 377,711. The incidence of anesthesia death during induction in the "non-curare" group is, then, 1:10,800, less than one-fifth as high as when "curare" is used in induction.* It seems impossible that the assumption of major-minor case distribution can be sufficiently in error to change the conclusion that there is a difference. This is a sharp indication that "curare" may be causing trouble.

Does the experience of the anesthetist protect against disaster with "curare"? We have considered three groups: physician specialists, residents in anesthesia and nurse anesthetists. Although the difficulty of cases handled by the physician specialist is usually greater than for the nurse, when both are available in the same institution, never-

* The incidence of fatal cardiac arrest in the ten participating institutions averaged 1:3000. This is based on 199 fatal cardiac arrests in 599,548 cases. In seven of these hospitals there was a rather marked consistency, near the average. It is probably fair to assume that if the incidence of *fatal* cardiac arrest is 1:3000, as we have shown, in these hospitals the cardiac arrest frequency is probably double this or 1:1500, since at the present time the staff in most university institutions is able to save about half of these cases.

TABLE XXII. *A. "Curare" Agent and Associated Deaths.**

Agent	Uses	Deaths	Rate
Tubocurarine Chloride	9,065	25	1 : 360
Decamethonium Bromide (Syncurine)	6,147	11	1 : 560
Succinylcholine Chloride (Anectine)	699	3	1 : 230
Gallamine Tri-Ethiodide (Flaxedil)	448	1	1 : 450
Dimethyl-Tubocurarine Iodide (Metubine)	201	0	0
	16,560	40	1 : 410

*Here counted are uses and associated deaths only where the curare-like agent was specified for all cases, both living and dead.

B. "Curare" Deaths.

Agent	Number* Uses in 118 Deaths	%
Tubocurarine Chloride	92	75
Chondodendron Tomentosum Extract (Intocostrin)	5	
Decamethonium Bromide (Syncurine)	25	19
Succinylcholine Chloride (Anectine)	3	2
Gallamine Tri-Ethiodide (Flaxedil)	2	2
Dimethyl-Tubocurarine Iodide (Metubine)	2†	2

*More than 118 since more than one agent used in some deaths.

†These deaths occurred in institutions at a time when they were not providing us with precise data on the "curare" agent used in all cases, hence they are not included in the A. part of the Table above.

theless, the comparison shown at the bottom of Table XVIII indicates comparability of good and poor risk cases in the three groups in the over-all data.

It would be unreasonable to deny the complexities of this situation. Common observation indicates that the physician specialist on the average cares for the patient faced with the more trying and difficult operation than does the nurse, even though both groups work with a comparable number of patients in poor physical status. This is supported by the data of Table XIX, where it can be seen that although the physician specialist anesthetizes only half as many patients as the nurse, he is charged with an equal number of anesthesia deaths. In the light of this, to deny the greater difficulty of the physician specialist's cases is to reduce the matter to an absurdity where one would be obliged to argue that the physician's learning was a dangerous thing. Granting, then, that the physician specialist does, indeed, in the university hospitals

TABLE XXIII. *"Curare Deaths" Rate and Experience with "Curare."*

	Uses	Deaths	Ratio
Large* Experience	33,900	92	1 : 370
Small* Experience	10,200	26	1 : 390
All Institutions	44,100	118	1 : 370
All Institutions Less One (Greatest User)	29,400	77	1 : 380
Greatest User	14,700	41	1 : 360

*Large is considered here as more than average (4,180) or more than 1,000 uses per year; small less than this.
Large users averaged 1,693 "curare" uses per year.
Small users averaged 341 "curare" uses per year.

involved here, care for greater problems than does the nurse, it is interesting that his *per cent* of anesthesia deaths which involved "curare" is exactly the same as his *per cent* of anesthesia deaths where no "curare" is used. The same is true for the nurse. This does not conflict with the fact that more deaths occur when "curare" is used. In Table XIX A, the data could be still more interesting if we had further information about the differential rates of "curare" use by the various anesthetists.

Many of the hazards of disease and the problems of therapy can be overcome by experienced and wise physicians. In some situations, notably those involving inherently toxic agents, however, wisdom and experience do not protect (however skillfully arsenic is administered, beyond a certain dose it kills, etc.), and the case of the muscle relaxants seems to be such a one, at least one where experience does not demonstrably protect.

Again, in Table XXIII, the institutions which averaged 341 uses of "curare" per year had as good a record in the use of "curare" as those which averaged five times as many (1693) cases per year. Experience of institution does not appear to lead to increased safety.

In our judgment the situation is one where neither experience of individual nor experience of institution appears to protect. This adds up to evidence that neither mistakes nor preventable error of any kind are involved in the main, but rather the inherent toxicity of the "curares" themselves.

TABLE XXIV. *Gross Errors in Anesthetic Management.*

	"Non-Curare" Deaths (266)	"Curare" Deaths (118)
Number	17	12
Per Cent	6%	10%
Modified* Death Rate	1 : 2200	1 : 420

*Obtained by subtracting number of gross errors from number of deaths and comparing the result with total cases in each category.

TABLE XXV. *"Curare" Deaths*

Primary Cause of Death

	Number Cases	Per Cent
Respiratory Failure (Hypoxia)	74	63
Cardio-Vascular Failure (notwithstanding artificial respiration)	44	37
		100%
Role of Anesthesia in Death*		
Toxicity of "Curare" (assumption) (no error apparent)	25	21
Error Technic "Curare's" Use (overdose, respiratory depression or obstruction not corrected)	37	31
Error Choice "Curare" (in severe respiratory impairment, shock, full stomach, where relaxation not needed)	20	17
Error Anesthetic Management (not directly related to "curare")	36	31
		100%

*The gross error incidence is shown in Table XXIV. These gross errors are included here, but also included here are other supposed errors, identified by hind-sight. Errors in anesthesia management not directly related to "curare" are included for completeness because the patients did get "curare" and died. There may even be a real connection with the use of "curare", for the anesthetist absorbed in watching "curare" effects, giving artificial respiration and so on may be less alert than otherwise to avoid errors of general anesthesia management.

One of the participating institutions was a far greater user of "curare" than the others, with a correspondingly large number of "curare deaths." It is clear from the data on this matter presented in Table XXIII that this institution did not distort the over-all data.

There appears to be a disproportionately high incidence of "curare" deaths in men. Even though physical status in the over-all data does not appear to be important so far as "curare" or no "curare" goes, it is still possible that certain pre-existing diseases may predispose to death when "curare" is used. Possibly the greater incidence of death in men is related to the higher incidence of serious heart disease in men than in women. The higher incidence of "curare" deaths in men (Table XXI) is compatible with evidence found in this study that "curare" may injure through circulatory collapse, even in the presence of adequate pulmonary ventilation (Table XXV). This higher rate in men may also be related to the greater age of the male patients in the "curare" death group. Or, to state this positively, the women of this study actually appear to tolerate "curare" better than men, for reasons that are not clear. In part, at least, the greater age of the patients labeled "curare" deaths is related to the fact that "curare" is not as much used in children as in adults. The interrelationships of these variables present problems too complex for definitive answers.

A good question is, are the "curare" deaths associated with recognizable *gross* misuse, with overdosage? The answer is "no" for most cases (the percentage of detected *gross* error is small), as shown in Table XXIV. Obvious, gross errors in anesthetic management occurred in 29 of the 384 anesthesia deaths, divided as shown in Table XXIV. Rigorous inspection of all of the "curare" deaths gave reason (by hind-sight in the central office) to suppose that various errors were committed as shown in Table XXV. It is clear that the gross errors do not account for any difference in the ratios between the two groups: the ratio of 1:420 to 1:2200 as shown here is not different from the ratio of 1:370 to 1:2100, for the over-all data. The higher death rate when "curare" is used thus cannot be accounted for by gross error, as suggested by some.

Another question is, how do these patients die? One must recognize the great difficulty in judging whether death, when it occurs rapidly, was due primarily to respiratory or to circulatory failure. It is sur-

TABLE XXVI. *Death Rates in Surgical Patients* Classified as to Cause.*

Based Upon 599,548 Cases

Cause of Death—Primary	Number	Rate
Patient's Disease	6,325	1 : 95
Surgical Error (in diagnosis, judgment, technic)	1,428	1 : 420
Anesthesia Death	224	1 : 2680
Total	7,977	1 : 75
Anesthesia, Primary and Contributory	384	1 : 1560

*Excludes patients who had no anesthesia and no operation (see Table XXVII), and includes patients with anesthesia without surgery.

TABLE XXVII. *Classification of Deaths on Surgical Services.*

Cause of Death	Anesthesia or Operation		No Anesthesia No Operation	
	Primary	Contributory	Primary	Contributory
Patient's Disease	6,325	991	5,355*	282
Error in Diagnosis	194	145	39	25
Error in Surgical Judgment	391	266	16	10
Error in Surgical Technic.	843	282	—	—
Anesthesia Death	213†	171†		
Anesthesia Deaths (Corrected)†	224	160		

*Neonatal deaths contribute largely to this number.

†This is the way the data were reported and are therefore recorded as sent in. The 171 "contributory" cases included, however, 11 patients who died during induction before surgery had started. This is an error of cataloguing, since the group of participants had agreed that by definition death during induction before surgery would be classified as an anesthesia death, not a very great assumption.

prising that so many die of failure of the circulation despite artificial respiration of a generally effective type (bag squeezing). This introduces a new element. It has not heretofore been clearly recognized that a common cause of death from "curare" is circulatory collapse. From these data this appears to be the case (Table XXV). It may be well to point out that we had no right to exclude the data in the last category of Table XXV, anesthesia deaths in the "curare" group not directly related apparently to the "curare." Even if the assumption was correct, for example, that an air embolus was the immediate cause of death, it is conceivable that a patient's circulatory system might have been so weakened by the "curare" that he succumbed when he otherwise would not, etc.

It is evident from Table XV that the most popular combination by far (85 per cent of the uses) is "curare" with nitrous oxide and thiopental (Pentothal). At the present time there is for some reason a wave of rather severe criticism of thiopental to be heard, perhaps in actuality more justly attributable to the "curare" often used with it than to the thiopental itself. The fact that this is to be heard rather than seen in the accompanying figures is beside the immediate point, but is incidentally an interesting commentary on the discrepancy between observed fact and current comment, to be discussed later. In any case, with such points of view around, it is useful to look at the data of Table XVI. It can be seen there that there is a steady and great improvement in the death rate associated with thiopental over the period of this study, and at the same time a grim constancy of death rate associated with "curare." These data are, to say the least, against the likelihood that thiopental (as we saw in Table XV, the agent most popularly associated with "curare") is to be charged with the major cause of these disasters. That this combination is not as bad as others is indicated by the data of Table XXXIII B. As shown there the combination of ether and "curare" appears to be far worse than the combination with thiopental. The combination of "curare" and cyclopropane also appears to be worse than the combination with thiopental. Lest there seem to be a discrepancy between Table XXXIII B and XXXI B, it must be recalled that in Table XXXIII B the *primary* agent—"curare" combination—is under consideration.

We have no wish to end this section with foolish, or extreme conclusions. How, then, can this matter be summed up? Deaths associated with all of the muscle relaxants studied (including the new succinylcho-

TABLE XXVIII. *"Anesthesia Death Rate."*

	Total Cases	Deaths	Ratio of Deaths to Cases
1948	108,100	75	1 : 1440
1949	117,800	80	1 : 1470
1950	123,600	89	1 : 1390
1951	122,000	72	1 : 1690
1952	128,000	68	1 : 1880
	599,500	384	1 : 1560

TABLE XXIX. *All "Anesthesia Deaths."*

Decade	1	2	3	4	5	6	7	8	9	10
Sample* Surgical Population	9	8	16	16	16	14	12	7	2	0.2
"Anesthesia Deaths" (384 Cases)	20	4	6	12	13	15	16	10	4	0.3

	Per Cent Race and Sex Distribution			
	White	Negroes	Male	Female
Sample* Surgical Population	70	30	43	57
"Anesthesia Deaths" (384 Cases)	72	28	58	42

*9300 patients in hospitals on 1 April 1950 and 1 February 1952.

line) have occurred under circumstances where the muscle relaxants themselves seem to have been important in the result. It is not yet clear whether there are real differences in death rate attributable to the several muscle relaxants. There seems to be an important increase in "anesthesia death rate" when the muscle relaxants are added to the situation. Evidence is presented that the "curare deaths" occur as often proportionately in patients in good physical status as in poor physical status. "Curare" deaths occur with minor surgery as well as with major. And again the death rate is six times higher in the "curare" group than in the no-"curare" group when major operations are compared. Neither experience of the anesthetist nor experience of the institution appears to protect the patient when "curare" is used. A new finding is that the muscle relaxants appear to play an important part in the death of a considerable number of patients through circulatory collapse, despite artificial respiration. This is in line with recent findings concerning the pharmacology of these agents (early ganglionic block). The incidence of clearly recognized *gross* misuse of these agents is so low that it can hardly be called an important factor in this situation. All of this adds up to the possibility that the real problem here is inherent toxicity of the muscle relaxants studied.

Having presented the foregoing evidence and comment, one can ask what, then, is to be done about these agents? Are they to be banned as a practical solution of the problem? We believe not. These data suggest strongly that great caution in the use of the muscle relaxants should be exercised, that the agents available at present be considered as on trial, and that they be employed only when there are clear advantages to be gained by their use, that they not be employed for trivial purposes or as a corrective for generally inadequate anesthesia.

With all of this evidence in hand, why do we not condemn "curare" absolutely? We do not because we recognize the possibility that conclusions based upon anesthesia death rate can be at variance with conclusions based on over-all surgical death rate. It is conceivable that an excess of anesthesia deaths could occur at the same time as a decrease in the over-all surgical deaths. If this occurred, the anesthetist, as part of the surgical team, would have to bear the stigma of an increase in deaths assigned to him as a part of the team. But presumably the team would benefit from decrease in deaths from patient's disease and surgical error. We are not at all convinced that such a hypothetical decrease in over-all death rate of surgical patients obtains with "curare," but as we mentioned earlier, our present data are not adequate to test this point. Even if this decrease did hold, the data we have presented make it

TABLE XXX. *Anesthetic Agents and Associated Deaths.*

Agent	All Uses	Deaths	Rate*
Nitrous Oxide	213,900	200	1 : 1070
Ether	177,900	218	1 : 820
Cyclopropane	74,700	85	1 : 880
Ethylene	52,500	31	1 : 1690
Vinyl Ether	36,200	29	1 : 1250
Thiopental (Pentothal)	144,700	161	1 : 900
Spinal Anesthesia	58,700	33	1 : 1780
Regional Anesthesia	165,300	71	1 : 2330
"Curare"	44,100	118	1 : 370

*Ratio of any agent used in "Possible Anesthetic Death" to all uses (including combinations) of this agent.

clear that students of anesthesia can well afford to search for means of reducing the *anesthesia* death rate associated with "curare."

Under more nearly ideal circumstances than ours, where only experienced teams work with a single anesthesia procedure and a single operation, say, it might be possible to show that the use of the muscle relaxants is good for the over-all death rate. Our survey in the ten university hospitals is less ideal than the above hypothetical situation; yet our university hospital circumstances are probably in turn more nearly ideal than the situations where the great bulk of clinical practice is carried out. It is certainly immediately desirable to get data to fill out the area where we do not know for sure whether or not "curare" might, in fact, be good or bad for the *over-all* surgical death rate.

DISCUSSION OF SPECIFIC DATA ON DEATH RATES OF SURGICAL PATIENTS

In this study, 599,548 patients on the surgical services of the ten participating hospitals who received anesthesia came under study. In this group there were 7977 deaths apportioned, as shown in Table XXVI. For completeness, an additional group of patients on the surgical services, with some 5727 deaths, very largely neonatal, who had neither anesthesia nor operation, is shown in Table XXVII. To return to Table XXVI, it is of interest to observe that the average patient who enters one of the ten participating hospitals and has anesthesia or surgery has one chance in 75 of dying from one cause or another. He has one chance in 95 of dying from "patient's disease," usually the disease which brought him in. Presumably nothing can be done about this, at least not until basic advances in medicine are made in the conquest of the diseases that afflict him. On the other hand, the patient has a right to expect that early improvement will be made in care leading to fewer deaths resulting from surgical mistake, whether due to errors in surgical diagnosis, technic, or judgment, as well as a lessening of deaths resulting from anesthesia errors. (Tables XXVI and XXVII present data on the incidence of death due to errors in diagnosis, surgical technic, and judgment, as well as anesthesia.) One mitigating factor is that with medical advances, patients who previously died at home, without blame to any surgeon, now may be brought to the surgeon for treatment. This must naturally increase the surgical death rate, because of the increased risk the surgeon takes to correct a difficult situation previously regarded as hopeless.

In order to avoid a false precision in the classification of deaths, from the beginning of this work, we allowed for the categories "primary" and "contributory," described above. As we have studied the death protocols it is apparent that while there would be general agreement as to those designated as primary anesthesia deaths, many would also have placed those labeled contributory in the primary category. These are matters of individual judgment. In Table XXVI we have given both kinds of data. We are agreed that in both categories anesthesia was a very important cause of death. (See the section above describing an anesthesia death.) These cases are the ones we have sought to single out. In all of the tables, unless otherwise designated,

TABLE XXXI.* *"Anesthesia Deaths."*

Number of Deaths Using A Single Agent or A Single Agent Plus Nitrous Oxide Only, Compared with Total Primary Uses of This Agent

A. Without "Curare"

Agent	Uses	Deaths	Rate
Nitrous Oxide	26,200	5	1 : 5200
Ether	171,300	68	1 : 2500
Cyclopropane	37,100	7	1 : 5300
Ethylene	29,200	2	1 : 14,600
Thiopental	14,000	6	1 : 2300
Thiopental-Nitrous Oxide	43,000	17	1 : 2500
Spinal	58,700	22	1 : 2700
Regional and Topical	152,000	20	1 : 7600
		147	

B. With "Curare."

Thiopental and/or Nitrous Oxide-"Curare"	38,100	49	1 : 780
Cyclopropane-"Curare"	2,400	2	1 : 1200
Ether-"Curare"	2,000	8	1 : 250
		59	

*This table is distinctly selective: all those "anesthesia deaths" in which more than nitrous oxide and a single agent were used, were empirically omitted; i.e., 59 (50%) of the "curare deaths" and 119 (45%) of the "non-curare deaths".

it is this combined group that we refer to. From the data provided in Table XXVI, the reader can recalculate, percentage-wise, the material of the other Tables, if he cares to do so.

Table XXVIII shows the yearly spread of the deaths where anesthesia was of great importance.

Data on sex, race and age are presented in Table XXIX.

Sex. It is interesting that the male-female relationship of anesthesia deaths is just the reverse of the sexes' representation within the hospitals' population, as shown in Table XXIX. This is doubtless accounted for in part by hospitalization of women for childbirth. Possibly men (the wage-earners) postpone hospitalization longer than women, with resultant poorer general physical status when they do come in. Perhaps the higher incidence of serious heart and circulatory disease in men makes them less able to tolerate anesthesia than women. Here is a field for further inquiry.

Race. In this connection there is a good lesson for us concerning the hazards of small samples: It early appeared as though deaths in colored (Negro) patients were disproportionately high considering their hospital representation. The incorrectness of that conclusion is shown in Table XXIX.

Age. The anesthesia death percentage is disproportionately high in the first decade of life. This indicates a great need for an attack on the anesthesia problems of infants and children. After the first decade, the anesthesia death percentage remains below the hospital age distribution until the sixth decade, when it begins to creep ahead. There is also need for special study of anesthesia for the aged. It might be said that the problem in the aged is merely one of impaired organs failing to withstand the stress of anesthesia. If that is the only problem, how is one to account for the disproportionately high death rate in children? Perhaps their immature organs are less able to withstand the stress of anesthesia than are those of healthy young adults. Doubtless, problems of ventilation are involved.

Tables XXX, XXXI, XXXII and XXXIII arose from a situation where there is a real problem, not only as far as this study is concerned, but in actual practice. It is plainly impossible to get at a precise statement of death rate for a specific agent when many agents are used together, when the rates do not differ by more than one or two hundred per cent. In the case of "curare," where something like a six-fold difference was elicited, the use of multiple agents is less important. This underscores an important point: when several or many agents are used together, it becomes extremely difficult, even nearly impossible, to determine which agents are causing trouble, unless the newly introduced agent is associated with a very high death rate. The common practice of using many agents in combination thus makes it exceedingly difficult to learn from experience, and constitutes, in this regard at least, an obstacle to progress.

TABLE XXXII. *Frequency of Death Associated with 599,500 Anesthesias.*

Anesthesias Which Included:	Anesthesias Which Did Include:
No "Curare" (266)* . . . 1 : 2100	"Curare" (118) . . 1 : 370
No Ether (166) . . . . . 1 : 2500	Ether (218) . . . . . 1 : 820
No cyclopropane (299) . 1 : 1800	Cyclopropane (85) . . . . . 1 : 880
No Nitrous Oxide (184) . . . . . 1 : 2100	Nitrous Oxide (200) . . . . . 1 : 1100
No Vinyl Ether (355) . . 1 : 1600	Vinyl Ether (29) 1 : 1300
No Ethylene (353) . . . . . 1 : 1600	Ethylene (31) . . . 1 : 1700
No Thiopental (223) . . . 1 : 2000	Thiopental (161) 1 : 900
No Spinal (351) . . . . . 1 : 1500	Spinal (33) . . . . . 1 : 1800
No Reginal (313) . . . . . 1 : 1400	Regional (71) . . . 1 : 2300

*Figures in parentheses represent numbers of anesthesia deaths.

Of the agents in Table XXXI A, ether and spinal anesthesia are employed in operations where muscular relaxation is essential, and have comparable death rates.

OTHER GENERAL OBSERVATIONS EMERGING FROM THIS STUDY

THE UNSETTLED CONDITION OF PRACTICES IN THE FIELD OF ANESTHESIA

It might have been supposed that any field of medicine which has existed for over a hundred years would have attained a considerable degree of stability in its practice. To point out that this is not the case in anesthesia is not to criticize adversely the laudable desire for improvement in existing ways of doing things, a desire which naturally leads to trial of new procedures. But it is evident in the material collected in this study that there is an extraordinary amount of turmoil present; rapid adoption of new technics, equally swift abandonment of the old. For example, in the short space of five years covered by this study, we find that ether increased in use 45 per cent, and the increase was steady. In the same period, use of the semi-open technic increased 60 per cent. The to-and-fro carbon dioxide absorption technic fell to one-fifth what its use had been. There was a more than three-fold increase in the use of controlled respiration. The use of dibucaine (Nupercaine) for spinal anesthesia fell to one-quarter what it had been at the beginning of the study. There has been a great decrease in the use of continuous or multiple dose spinal anesthesia. Tetracaine (Pontocaine) has fallen to half the topical use it had. Endotracheal intubation has more than doubled as an adjunct of intravenous anesthesia in these five years. One could go on at considerable length, but to no further purpose. Surely these observations add up to evidence that there is in the field of anesthesia too often too great haste to praise and to blame. There is, certainly, need for more and better evidence for adopting or rejecting a given practice than sometimes is allowed to suffice. There is an understandable tendency to rebel at the mass of data needed for sound conclusion in this field. Rather than to ignore or deny this need, it would be more profitable to face it.

DISCREPANCY BETWEEN PREVALENT BELIEFS AND FACT

It is believed that the ten institutions participating in this study come as near representing informed and progressive practice in the field of anesthesia as can be obtained on a large scale. If this assumption is correct, it may be of interest to compare several common statements with the facts as elicited by this work. While many examples could be found, five will be mentioned here.

The Place of Ether Anesthesia. Many able men appreciate this agent, but there is also a very great number who speak of it either in the past tense or contemptuously as something for the novice, but not the expert to use. The fact is, primary use of the agent increased steadily 45 per cent during the five years of this study. Alone, or in its various combinations, it was used in 62 per cent of all primary inhalation anesthesia in these ten university hospitals.

The Place of Cyclopropane Anesthesia. This interesting agent has suffered much

from its friends. Only a few years ago, every couple of months or so an article appeared extolling this agent as the solution for most anesthesia problems. A good deal of this over-statement lingers, and one still hears it occasionally; therefore, it must come as a surprise to find that the primary use of cyclopropane is falling (the number of uses remains about the same, despite the fact that an 18 per cent increase occurred in the over-all number of anesthesias administered), and amounts to only 12.5 per cent of primary uses, and is limited to 18 per cent when its use in combination with other agents is included. Thus it is used less than one-third as often as ether.

The Muscle Relaxants ("Curare"). There are two schools here: one strongly for, one against. The former is by far the larger, and often denies any hazard in the use of these agents above that associated with any anesthesia procedure. The problem is a complex one; but we think this optimistic view is not supported by the "curare" data presented above.

The Nurse Anesthetist. One can often hear that the nurse anesthetist is a blight, that her day is over, that she is no longer needed. While the large teaching hospitals involved in this study might possibly be able to staff their departments entirely with physicians, it is by no means certain that they could and still maintain the same high level of staff and resident material throughout. This is speculation. The fact is, they have not all chosen to do so. Whatever the future of the nurse anesthetist may be, she remains an important part of the university teaching hospital world, caring as she does for a fifth of all anesthesias in these hospitals, twice as many as physician specialists in anesthesia. Her importance in countless small hospitals is even greater; in many of these she administers all anesthesia.

The Death Rate Attributable to Anesthesia. Text books, as well as common statement, can be used to support fantastic assertions as to the safety of anesthesia. One need expect only one death in 5000, in 10,000, in 15,000 cases, so it is said. These statements compare poorly with the finding in the 599,548 cases of this study, of one anesthesia death (deaths where anesthesia was an important factor; *i.e.*, "primary," plus important contributing cause) in every 1560 anesthesias. This seems to us like the soundest way to look at these data. However, if he chooses, one can look at the "primary" anesthesia deaths alone; in this case the rate is 1:2680 (Table XXVI). This is of questionable wisdom, since judging from the protocols sent in, there is little, if any, difference between the make-up of the two groups.

There is an understandable, if unsound, reluctance to grant that large numbers are necessary to get at the truth of anesthesia deaths. It has many times been firmly stated when the results of this study were being discussed, "well, whatever that study shows, my experience is nothing like as bad, etc., etc." In this connection it is interesting to recall that even within the groups participating in this study, one of the participants accepted the first year's report with equanimity, likewise, the second year's report; but when a three-year summary of their own data was sent to them, they were not willing, at first, to believe they could have had so many anesthesia deaths, even though they had so classified their cases at the time they occurred. This is a revealing experience. It is not surprising that those who have never accumulated carefully large quantities of data, have a "clinical impression" at variance with the facts.

DEATH FROM ANESTHESIA AS A PUBLIC HEALTH PROBLEM

Any agent or agency which regularly and systematically injures a considerable number of citizens each year is a public

health problem, whether it be the virus of poliomyelitis, or the family automobile in a crash, or, as in this case, anesthesia. The significance of the problem, in national terms, depends largely upon its size. If this is found to be considerable, the problem merits national assistance to overcome it, and sound attacks on it deserve national support.

It will be profitable to take a good look at the problem of anesthesia deaths from this point of view. Let us assume, for the moment, that the death rate from anesthesia throughout the 6000 reporting hospitals of this country is no higher than it is in the ten excellent departments of anesthesia involved in this study. This is a very tall assumption, but since it leads to understatement of the conclusion to be arrived at, we can accept it for illustrative purposes.

Take poliomyelitis as an example. The average incidence* of death from this disease in the United States during the five years of this study was 1.38 per 100,000 of the population. From information supplied by the American Hospital Association,† there are approximately 8,000,000 anesthesias (operations) in hospitals each year in the United States. With a death rate of 1:1560 associated with anesthesia, there were each year, therefore, 5128 anesthesia deaths in a total population of 156,000,000; that is, an incidence of death associated with anesthesia of 3.29 per 100,000 of population. Thus there were 2.4 times as many deaths each year attributable to anesthesia in the total population of the United States during the five years of this study as there were deaths attributed to poliomyelitis.‡

Anesthesia might be likened to a disease which afflicts 8,000,000 persons in the United States each year. More than twice as many citizens out of the total population of the country die from anesthesia as die from poliomyelitis. Deaths from anesthesia are certainly a matter for "public health" concern.

When one thinks of the millions of dollars rightly spent each year on research to combat poliomyelitis and the next-to-nothing, comparatively, spent in research to overcome the hazards of anesthesia, a very great need is evident.

Summary

Summary of the Plan of the Study

Ten teams, consisting of an anesthetist, a surgeon and a secretary, worked for a five-year period in ten university hospitals scattered widely over the United States. *All* deaths occurring on all of the surgical and surgical specialty services were examined and appraised as to cause of death by the team working in each of the participating hospitals. Final decisions were made by the local team in each hospital, usually after full staff discussion. These decisions were made as soon after each death as the relevant material could be assembled by those who were on hand at the

* Calculated from data supplied by Dr. Robert E. Serfling, Chief, Statistics Section, Epidemiology Branch of the Public Health Service, Department of Health, Education and Welfare, United States Government. Both of these gentlemen have our cordial thanks for their help.

† Courtesy of Mr. Bremen I. Johnson, who supplied information on non-reporting hospitals. See also *Hospitals*, Part II, June, 1950.

‡ Deaths from poliomyelitis often vary widely from year to year. On the other hand it is probable that the anesthesia death rate is steady, showing only gradual change. (The poliomyelitis death rates were unusually high during the five years of this study.) The soundest comparison, then, can be made by taking the average poliomyelitis death rate over, say, the last 20 years. For this period it is 0.9 per 100,000 of population, that is, the death rate associated with anesthesia is more than three times that of poliomyelitis. Early reports of this comparison were made to the participants, based upon the poliomyelitis death rate for the year the study was planned (1947), 0.4. That year the deaths associated with anesthesia were eight times those from poliomyelitis. The 20-year average referred to above was derived from data presented by Serfling and Sherman.[3]

time the death occurred. It is to be emphasized that in this study there was nothing voluntary or selective about reporting of the deaths, once an institution with its team had agreed to participate. A point is made of this fact, since studies of intermittently or casually, or partially reported deaths can never get to the center of a problem of this kind. *All* deaths were categorized and reported. The designation as to cause of death was made in the institution where it occurred; this classification was not altered in the central office.

Reports to the central office were made at four-month intervals by each of the participating hospitals; thus each institution sent in 15 reports over the five-year period. In these reports, the cause of death was characterized as due to patient's disease, error in diagnosis, error in surgical judgment, error in surgical technic or anesthesia death. For two weeks during each four-month period, the numbers of certain key operations were tallied in order to check the uniformity of the surgical material in the ten institutions. A sampling of the ages and races of the patient material was made on all patients present in the ten hospitals on two dates considered representative.

From the data collected on 599,548 anesthesias, the following observations can be made for the period of this study.

SUMMARY OF DATA ON AGENTS AND TECHNICS

1. A fifth of the anesthesias in these ten university hospitals are administered by nurses; *i.e.,* twice as many as are administered by physician specialists in anesthesia. On the other hand, in the five-year period of this study, while the number of anesthesias increased 18 per cent, those administered by nurses increased by only 3.5 per cent (a relative decrease), whereas those given by physician specialists increased 34 per cent, and those given by anesthesia residents increased 40 per cent. This reflects the current trend (Table I).

2. Inhalation anesthesia is by far the single most important technic; but the use of intravenous anesthesia has doubled in the period of study, while the use of the spinal technic has declined somewhat. It accounts, surprisingly, for less than 9 per cent of the cases (Table II).

3. The use of ether as a primary anesthetic agent is steadily increasing (Table III), while the use of cyclopropane is not rising. Ether alone or in its various combinations is used three and a half times as often as cyclopropane alone or in its various combinations.

4. The closed, circle filter arrangement has acquired and held an important place; but in the period of this study there has been a great increase in the semi-open technic. There has been a great reduction in the use of the to-and-fro filter. The tremendous increase (Table IV) in the use of "controlled respiration" probably has been required by the widespread use of the muscle relaxants.

5. Most spinal anesthesia is carried out with tetracaine (Pontocaine) or procaine. There has been a sharp decline in the use of dibucaine (Nupercaine) in the five years (Table VII). Heavy solutions are far more widely used than are light ones. The continuous or multiple dose technics of spinal anesthesia have greatly decreased in use during the course of this study.

6. Procaine is by far the most commonly used agent for local or regional anesthesia. The use of cocaine for topical anesthesia has remained steady over the last four years, whereas the use of tetracaine (Pontocaine) for this purpose has sharply fallen (Tables IX and X) in the period of this study.

7. Endotracheal intubation is used principally with inhalation anesthesia; but there has been a very great increase in its use as an adjunct to intravenous anesthesia; probably this is a reflection of the employment of this combination with muscle relaxants

(Table XI). In this study as elsewhere, cuffs on tubes, although indicated for certain procedures, are found to have a mortality of their own.

SUMMARY OF DATA ON MUSCLE RELAXANTS ("CURARE")

1. Where there was sufficient data to judge, no impressive differences in death rate among the several muscle relaxants were observed here. While the data are too few to permit establishment of rates for the newer agents, death has occurred in association with each, including the new succinylcholine. No pretext is made of being able to spot a "curare" death apart from what has been defined as an anesthesia death. The significant point is that when the muscle relaxants enter the situation, the anesthesia death rate increases nearly six-fold, from an anesthesia death rate of 1:2100 (based upon 266 anesthesia deaths) to a rate of 1:370 (based upon 118 anesthesia deaths in 44,100 patients who received "curare"). These data suggest that the widespread custom of using "curare" for many trivial purposes is not justified (Tables XIII and XXII). It is also worth observing that death during induction of anesthesia occurred 35 times in 555,548 cases, a ratio of 1:15,500, when no muscle relaxants were used; and 21 times in 44,090 cases, a ratio of 1:2000, when muscle relaxants were used. A more accurate picture is doubtless presented when only the general anesthesias (68 per cent of the total) are considered; *i.e.*, 377,700. In this case there was an incidence of anesthesia death in the "non-curare" cases of 1:10,800, one-fifth as high as in the "curare" group. This is a sharp indication of danger in the use of the muscle relaxants.

2. Evidence is presented that "curare" is not customarily reserved for difficult or "bad risk" cases; *i.e.*, patients in poor physical status. The physical status of each patient was recorded *before* anesthesia. Of the patients who received "curare," 87 per cent were labeled as good risk, that is good physical status, and 13 per cent as bad risk. These figures compare well with 89 per cent and 11 per cent, respectively, in patients who received no "curare." Certainly, "curare" is not reserved for bad risk patients (Table XVII).

3. Data are presented which indicate that when "curare" is used, death occurs in the same ratio, good risk group to bad risk group of patients, whether "curare" was used or not. This strongly suggests an inherent toxicity, not a selective killing of the bad risk patient. (Certain specific diseases may predispose to death from these agents [Table XVII].)

4. Death associated with "curare" is not limited to situations where major surgery is involved (Table XIV).

5. Several categories of anesthetists are involved in this study, from nurse to physician specialist. No evidence is detectable that experience or training of the anesthetist protects from disaster with "curare" (Table XIX).

6. The participating institutions were divided into two groups, depending upon whether they were great or light users of "curare." There was no difference in the death rate associated with "curare" between the two groups. Thus experience of institution, like experience of anesthetist, fails to protect (Tables XIX and XXIII).

7. There appears to be a disproportionately high incidence of "curare deaths" in men. This is discussed (Table XXI).

8. Obvious, gross errors in anesthetic management, while occurring nearly twice as often within the "curare" group, were such a low percentage of the total groups involved as not to influence the results to any great degree (Table XXIV).

9. A new observation is made here that, despite artificial respiration of a generally effective type (bag squeezing), many "curare" patients die of circulatory collapse. It has not, heretofore, been recognized that

a common cause of death from "curare" is circulatory failure.

10. Evidence is presented that the combination of "curare" and thiopental (Pentothal) is not as dangerous as the combination with ether or cyclopropane (Table XXXIII).

On the basis of the foregoing observations one can ask what, practically, seems to be a sensible attitude toward the clinical use of the muscle relaxants? We do not believe that they should be banned, but that they should be studied further. Advances apparently are being made. For example, there is the desirable fleeting action of the new succinylcholine. The data presented strongly suggest that great caution in the use of the muscle relaxants is indicated, that the agents available at present be considered as on trial, and that they be employed only where there are clear advantages to be gained by their use, that they not be employed for trivial purposes, or as a corrective for generally inadequate anesthesia.

SUMMARY OF SPECIFIC DATA ON DEATH RATES OF SURGICAL PATIENTS

1. In this study of 599,548 surgical patients, spread over ten university hospitals scattered throughout the United States, a patient has a chance of 1:75 of dying from one cause or another. He has a chance of 1:95 of dying from the disease which brought him to the hospital. The rôles of errors in diagnosis, surgical technic and surgical judgment, as well as anesthesia, are shown in Tables XXVI and XXVII. The over-all anesthesia death rate is 1:1560 (Table XXVIII). The definition of an anesthesia death must be a fairly arbitrary matter. We defined this as well as we could before the study began. The figure just given represents cases where it was agreed that anesthesia was important in the death. Judging from the protocols sent in, there was little difference between the two groups, primary anesthesia death, and death where anesthesia was described as an important contributory cause of death. The 1:1560 represents the two categories. If only the cases labeled as primary anesthesia death are considered, the rate is 1:2680.

TABLE XXXIII. *Deaths Associated with Primary Agents.*

A. Without "Curare": Primary Agent Used in an Anesthetic Death Compared to Number of Primary Uses of this Agent

Agent	Uses	Deaths	Rate
Nitrous Oxide	26,200	6	1 : 4400
Ether	171,300	159	1 : 1100
Cyclopropane	37,100	16	1 : 2300
Ethylene	29,200	2	1 : 14,600
Thiopental	14,000	7	1 : 2000
Thiopental-Nitrous Oxide	43,000	24	1 : 1800
Spinal	58,600	30	1 : 2000
Regional and Topical	152,000	25	1 : 6100

B. With "Curare": Primary Agent-"Curare" Combination Used in Anesthetic Death Compared with Primary Uses of this Combination

Thiopental and/or Nitrous Oxide-"Curare"	38,100	57	1 : 670
Cyclopropane-"Curare"	2,400	10	1 : 240
Cyclopropane-Ether-"Curare"	1,600	16	1 : 100
Ether-"Curare"	2,000	32	1 : 62

2. One purpose of this study was to determine, if possible, comparative anesthesia death rates associated with the commonly employed anesthesia agents. The problem is attacked from various directions in Tables XXX, XXXI, XXXII and XXXIII. It is plainly impossible, even in a series as large as this, to get an accurate statement of death rate for a specific agent where many agents are used together, according to the current custom, unless the rates differ by several hundred per cent (as in the case of "curare"). The common practice of using many agents in combination makes it exceedingly difficult to learn from experience and constitutes, in this regard at least, an obstacle to progress.

3. Men appear to have a disproportionately high anesthesia death rate. Possible reasons for this are discussed (Table XXIX). Anesthesia deaths are not more common in Negroes than in whites.

4. There is a good deal that is of interest in the data on age (Table XXIX): Anesthesia deaths are disproportionately great in the first decade of life and in the later decades. This is a clear indication of the need for study of causes in these areas.

SUMMARY OF OTHER GENERAL OBSERVATIONS EMERGING FROM THIS STUDY

1. Great changes in the use of anesthesia agents and technics occurred within the five years of this study. This suggests that the practice of anesthesia is far, as yet, from achieving stability.

2. The inaccuracies of "clinical impression" in this field, as opposed to the evidence of carefully recorded fact, is illustrated by five examples: the place of ether anesthesia, the place of cyclopropane anesthesia, hazards in the use of muscle relaxants "curare"), the usefulness of the nurse anesthetist and, finally, the death rate attributable to anesthesia.

3. Data are presented to show that death from anesthesia is of sufficient magnitude to constitute a public health problem. Anesthesia kills several times as many citizens each year out of the total population of the country as does poliomyelitis. Consideration of the millions of dollars rightly spent in attacking poliomyelitis and the next-to-nothing, comparatively, spent in anesthesia research makes clear an urgent need.

In conclusion, we have not supposed that we could settle all of the problems encountered in this broad survey. Besides the amassing of a large body of much needed factual data described above, we believe we have had some success in three general areas:

(a) In stimulating renewed interest of other groups in these problems.

(b) In marking out more clearly than had been done before, the essentials of a study of this kind. While the basic structure of this is evident in the description of our methods, in this summarizing section it will be well to emphasize certain notable points which in the past have been often overlooked. In work of this kind it is necessary to deal with *all* patients, living and dead, within the area of inquiry. Even if a limited goal be pursued, such as death rate for anesthesia or for specific agents or technics, *all* deaths must be examined and recorded in the proper categories, not just those believed at once to be associated with anesthesia. This requires continuity of study, and clearly indicates as of little use studies which have depended upon intermittent and partial reporting of material. It also indicates as of relatively little use studies which have as their basic material only obvious, flagrant errors or accidents. It is also clear in this area, where it is difficult to eliminate bias, that study groups should be equally represented by surgeon and anesthetist working as a team. It is important that studies of this kind be made with as few preconceived ideas as possible, *i.e.*, not made to prove a point. The data must be amassed at the time they arise, not from records grown cold. And, finally, some indication is given in this study of the large quantities of data that are essential.

It is apparent that the best answers to certain kinds of questions can be obtained by limiting the inquiry in future studies to certain kinds of severe test situations (anesthesia for gastric surgery or for common bile duct surgery, etc.). It is clear in studies of this kind that great interest attaches not only to the number that die under the circumstances being studied, but also to how many live, and in those who die, all causes of death must be examined. A study directed along these lines might be able to show that the over-all death rate was smaller when some agent or technic was employed than when it was not. A sharp focus of this kind will, within its own limitations, probably give better information on specific details than is possible with a broad survey of the type we have carried out here.

(c) Again and again in the preceding pages we have pointed out specific areas worthy of ardent attack: for example, the question of why the anesthesia death rate is so disproportionately high in the first decade of life, as well as why it is high in the last decades of life. The whole matter of the proper place, the advantages and hazards of the muscle relaxants will bear far more study than has yet been possible. The need of support for research in this field of anesthesia is evident. Some data have been provided as to the inaccuracies of "clinical impression" as opposed to evidence derived from carefully recorded fact. There is great need for an attack on the problem as to how to make anesthesia safer for the patient while yet satisfactory for the surgeon and as comfortable as before for the patient. Our concern in this study has been to state what the given situation is, not what it should be. Subsequent studies could profitably be directed toward the latter problem: not how things are, but how they should be.

We wish to express our appreciation to Professor Frederick Mosteller for the discerning help he gave us from time to time on problems that arose during the course of this study.

We would be remiss if we failed to express our warm thanks to all of those who have patiently worked with us over the years of this study, tiresome and exasperating and rewarding as it has been. Through it we can see some of the shortcomings of anesthesia, as well as its strong points. The prospect for sound growth lies in such appraisal.

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* All dates are inclusive

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BOOK REVIEW

LIVING WITH A DISABILITY. Hoard A. Rusk, M.D., and Eugene J. Taylor, in Collaboration with Muriel Zimmerman, O.T.R., and Julia Judson, M.S. The Blakiston Company, New York, 1953.

Dr. Rusk has initiated a most useful study, the results of which are recorded in the volume under review. In it are illustrated a wide range of devices of substantial value in achieving the independence of those who are physically disabled through neurological disease, arthritis or amputations. Additionally, the sources from which this equipment can be obtained are listed alphabetically under "Picture Credits." By stating that, wherever possible, it is better to do things without special equipment, Dr. Rusk clearly indicates that he is aware of the place of such devices in the life of the disabled.

One wonders if the study which lists 282 devices, of which all but eight originated in the United States, indicates the absence of such equipment elsewhere, or whether the search was not extended much beyond North America. The omission of the simple hydraulic lift, manufactured by Hoyer, would seem to be a shortcoming, for this lift certainly simplifies the home care of a seriously disabled individual. Likewise, a very useful modification of a urinal consists of a condom connected to the urinal bag or bedside bottle for night use. Although this is universally used on this continent, mention is not made of it.

The book will prove very useful to all those who are engaged in teaching the seriously disabled patient to achieve independence.

A. T. JOUSSE, M.D.

AUTHOR'S CORRECTION

The following is a correction of the first paragraph of the article entitled "Factors Influencing the Survival of Successful Skin Homografts in the Chicken: I. Effects of Varying Age of Donor and Recipient," by Drs. J. A. Cannon, R. A. Weber, and W. P. Longmire, Jr., which appeared in ANNALS OF SURGERY, **139:** 468, 1954.

The corrected first paragraph reads as follows:

In a previous communication a technic of skin homografting in young chickens was described.[1] When this technic was used for homografts between chicks within the first 72 hours after hatching, 13 to 16 per cent of the homografts survived beyond the eighth postoperative week, and 5 to 10 per cent survived permanently (over one year).